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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,316	04/26/2001	Evi Kostenis	38005-147	5658

26633 7590 04/02/2003

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1646	16

DATE MAILED: 04/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/842,316	Applicant(s) Kostenis et al.
	Examiner John Ulm	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 22, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above, claim(s) *15 and 20-31* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-14, 16-19, and 32* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *14*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1) Claims 1 to 32 are pending in the instant application. Claims 1 to 10, 16 to 19 and 32 have been amended as requested by Applicant in Paper Number 13, filed 22 January of 2003.

2) Claims 15 and 20 to 31 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 11.

3) Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5) The instant specification does not comply with 37 C.F.R. § 1.84(U)(1), which states that partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. Figure 1 of the instant application, for example, is presented on five separate panels which do not form one complete view. The two sheets of drawings which are labeled "FIG. 1A-1" and "FIG. 1A-2" in the instant specification should be renumbered "Figures 1A and 1B". Figures 1B, 1D-1 and 1C-2 should be renumbered Figures, 2, 3A and 3B, respective. The rest of the figures should be renumbered accordingly Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

6) Claim 19 stands objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim for those reasons of record in section 7 of Paper Number 12. Applicant's assertion that the amendment to this claim has avoided this objection is groundless.

7) Claims 1 to 4, 8, 10 to 14, 16 to 19 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims encompass an isolated polynucleotide encoding a polypeptide having EDG8 biological activity. The text on page 14 of the instant specification states that "[b]y "EDG8 biological activity" is meant that the molecule is a functional receptor for S1P, LPA, dHS1P and related lysophospholipid mediators". The breadth of the instant claims is not supported by the instant specification because the only protein described in the instant specification which is a functional receptor for S1P, LPA, dHS1P and related lysophospholipid mediators comprises the entire amino acid sequence presented in SEQ ID NO:2 of the instant application. Applicant is advised that, because three nucleotide bases (a codon) encode a single amino acid and the alteration of a single base in a codon can change the amino acid encoded thereby, the alteration of 10% of the nucleotides in a coding region of a polynucleotide can result in the alteration of 30% of the amino acids encoded by that coding region. Whereas claim 1 encompasses an isolated polynucleotide encoding an amino acid sequence which can deviate from SEQ ID NO:2 by as many as 120 residues out of 399, the instant specification does not provide

the guidance needed to alter SEQ ID NO:2 at even one residue. Because the instant specification does not disclose whether the term "polypeptide having EDG8 biological activity" is limited to naturally occurring proteins or if it also encompasses synthetic proteins, one must assumed that these claims encompass an isolated nucleic acid encoding any protein having an amino acid sequence with at least 70% sequence identity to that single EDG8 amino acid sequence presented in SEQ ID NO:2 of the instant application, wherein that protein can function as a receptor for receptor for S1P, LPA, dHS1P and related lysophospholipid mediators. These claims encompass nucleic acids encoding literally tens of thousands of embodiments of non-naturally occurring proteins for which the instant specification does not provide even a single working example. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Because the instant specification does not identify those amino acid residues in SEQ ID NO:2 which are critical to the structural and functional integrity of a receptor for S1P, LPA, dHS1P and related lysophospholipid mediators, and those residues which are expendable, identify a structurally related protein for which this information is known and can be applied to the protein encoded by the claimed polynucleotide by analogy, or provide even a single working example of an EDG8 protein having other than a native amino acid sequence, one can not produce a protein having "greater than 70% homology" to that single EDG8 amino acid sequence provided by the instant specification and predict "by resort to known scientific law" if the resulting protein will function as claimed. A protein of the instant invention is a member of the family of receptor proteins known in the art as G protein-coupled receptors. Members of this family are defined by their very complex structure, comprising four extracellular domains, seven transmembrane domains and four cytoplasmic domains. Given this complex structure, an artisan could not reasonably expect to change even one amino acid residue in such a protein and produce a protein which retains both structural and functional integrity, much less the 120 residue changes permitted by the instant claims.

8) Claim 9 stands rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for using any "fragment" of SEQ ID NO:1 for those reasons of record in section 8 of Paper Number 12. Contrary to Applicant's assertion, nothing in the text on pages 15 and 16 of the instant specification excludes dinucleotides from the limitation "fragment". The text "preferably have at least 10", and the text "which are at least

about 10" preceded by "For instance" does not exclude two since these terms are exemplary, not exclusive.

9) Claim 16 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for those reasons of record in section 9 of Paper Number 12. As stated therein, this claim is directed to a process of producing a polypeptide comprising the amino acid sequence of SEQ ID NO:2 by culturing a host cell. However, the claim is not limited to a process which employs a host cell containing a polynucleotide encoding SEQ ID NO:2.

10) Claim 32 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim is directed to a pharmaceutical composition comprising a polynucleotide encoding "EGD8". The limitation "pharmaceutical composition" inherently implies a clinical utility. However, the instant specification lacks the guidance needed to produce a "pharmaceutical composition" comprising a polynucleotide and having a clinical utility. Applicant has traversed this rejection on the premise that gene therapy is a routine practice in the art, and cites five publications in support of this assertion. As stated in the original rejection, there is not a single publication of record which describes the effective administration of a polynucleotide encoding all or a portion of any member of the G protein-coupled receptor family to any mammal

for clinical effect. An argument that it is routine to do that which has never been done is not persuasive. Further, the publications cited by Applicant in support of this argument have not been considered because they are not of record.

11) Claims 1 to 14, 16 to 19 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11.1) Claim 17 is vague and indefinite because the identity of the "polypeptide" referred to therein is unspecified.

11.2) Claims 1 to 4, 8 to 14, 16 to 19 and 32 are 18 and 32 are vague and indefinite in so far as they employ the term "EDG8" as a limitation for those reasons of record as applied to claims 18 and 32 in section 11.2 of Paper Number 12. As stated therein, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of "EDG8" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

12) Claims 1 to 14 and 16 to 19 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by each of the Glucksmann et al. (WO 00/11166 A1, 02 Mar. 2000) and Behan et al. (WO 00/22131, 20 Apr. 2000) patent publications for those reasons of record in section 13 of Paper Number 12. As stated therein, the amino acid sequence presented in SEQ ID NO:2 of the instant application appears to be identical to the amino acid sequence presented in Figures 1A and

1B of Glucksmann et al. and amino acid residues 104 to 500 in SEQ ID NO:32 of Behan et al. Applicant's argument that the additional limitation "wherein the polypeptide has EDG8 biological activity" distinguishes the claimed polynucleotide from those that were described in these two references is incorrect. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) (M.P.E.P. 2112.01).

13) Applicant's arguments filed 22 January of 2003 have been fully considered but they are not persuasive for those reasons given above.

14) Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1800